https://doi.org/10.33004/reumatizam-supp-71-1-16

DIFFICULT TO TREAT PSORIATIC ARTHRITIS
"DIFFICULT TO TREAT" PSORIJATIČNI ARTRITIS

Ennio Lubrano [1]

[1]*Professor of Rheumatology, University of Molise, Campobasso, Italy.*

Psoriatic arthritis (PsA) is a complex immune-mediated condition characterized by musculoskeletal inflammation (peripheral and axial arthritis, dactylitis, enthesitis), extra-musculoskeletal manifestations (skin psoriasis, nail involvement, IBD, uveitis), and a wide array of comorbidities (metabolic syndrome, cardiovascular disease, mental health disorders, fibromyalgia). Despite advances in therapy, a significant subset of patients fails to achieve satisfactory outcomes. The concept of difficult-to-treat PsA(D2T-PsA)(1) is currently being refined, as it is critical for clinical trials, therapeutic strategies, and personalized care.

Recent studies have proposed varying criteria to define D2T-PsA. For example, Kumthekar et al. (2) suggest it includes failure of at least three bDMARDs or tsDMARDs and persistent problematic symptoms perceived by either the patient or physician. Across-sectional study compared two definitions (Perrotta et al. vs Kumthekar et al.) (3-4) and found low sensitivity but high specificity, with substantial agreement (kappa ≈ 0.74), indicating overlap in identified patient groups. A statistical model also identified a smaller subset of patients (2.9% to 17.2%, depending on criteria) who met D2T thresholds, with associated risk factors including fibromyalgia, nail or pustular psoriasis, corticosteroid use, and female sex.

In 2025, GRAPPAintroduced formal definitions of complex-to-manage (C2M-PsA) and treatment-refractory (TR-PsA), developed using a rigorous methodology with global input from clinicians and patients. C2M-PsAis defined as persistent symptoms despite at least one adequate trial of a b/tsDMARD, while incorporating comorbidities and psychosocial factors. TR-PsA, on the other hand, requires failure of ≥ 3 agents with different mechanisms of action (including two or more b/tsDMARDs), persistent problematic symptoms (clinician/patient reported), and objective evidence of inflammation.

EULAR has proposed a parallel framework: Difficult-to-Manage PsA(D2M-PsA) is defined by resistance to ≥ 2 b/tsDMARDs with different mechanisms of action, unsatisfactory response perceived by clinician or patient, and at least one of the following: failure to reach low disease activity, active extra-musculoskeletal manifestations, or objective evidence of inflammation. Treatment-Refractory PsA(TR-PsA) per EULAR requires therapeutic resistance, objective inflammation, and exclusion of comorbidities or psychosocial confounders (4).

These definitions received high internal consensus (95% in GRAPPA; 88–100% in EULAR) and now provide a structured foundation for future trials, registry studies, and real-world management. Comparative evaluation of the GRAPPAvs EULAR frameworks will further shape clinical applicability and therapeutic precision in PsA.

More recently, a different approach looking at D2T patients with persistent inflammatory signs at ultrasound compared to those D2T without persistent inflammatory manifestations has been published, paving the way for two potential D2T phenotypes (5,6).

Keywords: psoriatic arthritis, outcome, treatment, disease activity, imaging
E-mail of the main author: enniolubrano@hotmail.com
Conflict of interest statement: The authors declare no conflict of interest.